

## Amendments to the Specification

At page 2, please replace paragraph 8 as follows:

C1 [0008] This invention relates to a group of novel sapogenins, their use in anti-cancer applications, and to a process for their production. More particularly, this invention pertains to a novel group of dammarane sapogenins, PAM-120, PBM-110 and PBM-100 (the ~~dammarane sapogenine~~ dammarane sapogenin structure in these three sapogenins is specifically clean of any sugar moieties (glycons) at any position and a hydroxyl at C-20) and PAN-20 and PAN-30 (the ~~dammarane~~ dammarane sapogenin structure has sugar moieties (glycons) but is free of hydroxyl at C-20), obtained by chemical cleavage of dammarane saponins. The invention also includes a novel application of the said sapogenins for anti-cancer treatment by using them separately or together, and/or jointly with other drugs, as well as to the process of producing these novel sapogenins. Said novel dammarane sapogenins show surprising anti-cancer effect when applied. In particular, the novel dammarane sapogenins show unexpected and superior activity against multi-drug resistant cancers.

At page 6, please replace paragraph 17 as follows:

C2 [0017] The method can comprise a pharmaceutically effective amount of PAM-120, ~~PAM-100~~ PBM-100, PBM-110, PAN 20 and PAN-30, with or without one or more pharmaceutically acceptable carriers. The active ingredient can be administered in a dosage of between 5 micrograms to 50 grams per 1 kg body weight per day. A preferred range is 50 micrograms to 5 grams per 1 kg body weight per day. The form of the composition can be selected from the group consisting of an orally administrable form, an injectable form, and a topically applicable form.

At page 6, please replace paragraph 20 as follows:

C3 [0020] The invention also pertains to a process of preparing a sapogenin which comprises producing a ginsenoside extract from plants selected from the group consisting of panax ginseng, panax quinquefol and panax notoginseng, and proceeding according to the following steps: (a) mixing the ginsenoside extract with water; (b) (i) mixing the ginsenoside extract and water with a short-chain (1-5 carbon) alkali-metal alcoholate solution or a hydroxide-ethanol solution to produce a mixture; and (ii) placing the resultant mixture in a reaction tank so that the resultant mixture

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can undergo chemical reactions under required high temperature and high pressure; or (c) (i) alternatively, mixing the ginsenosides extract with ethanol; (ii) mixing the extract and ethanol with alkali-metal alcoholates solution to produce a mixture, and (iii) placing the resultant mixture in a reaction tank so that the resultant mixture can undergo chemical reactions under required high temperature and high pressure; (d) after the reaction is completed, collecting an intermediate product of a mix of ~~gensenosides~~ ginsenosides and sapogenins from the ethanol mixture; and (e) separating the desired sapogenins from the intermediate saponin-sapogenin mixture by silica-gel-column chromatography.

At page 7, please replace paragraph 21 as follows:

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**[0021]** The alkali metal can be potassium or sodium. The hydroxide can be sodium hydroxide or potassium hydroxide. The alkali-metal alcoholates solution or the concentration of hydroxide-ethanol solution can be 5~50% (W/V). The alcohol can have 1~5 carbon atoms. The temperature of the reaction tank can be between 150~300°C and the reaction pressure can be between 2.5~8.4 MPa. Preferably, the temperature is between 240-300°C and the pressure is between 3.5~8.4 MPa.

At page 8, please replace paragraph 31 as follows:

**[0031]** This invention relates to a physically obtained group of novel compounds as follows:

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- Dammara-20(21)-diene-3,12-diol (named as PAM-120);
  - Dammara-20(22E)-diene-3,12,24-triol (named as PBM-100);
  - ~~Dammara-2-(22E)-diene-3,6,12-triol~~ Dammara-20-(22E)-diene-3,6,12-triol (named as PBM-110);
  - 3-O-β-D-glucopyranosyl-dammara-20(21)-diene-3,12-diol (named as PAN-20); and
  - 3-O-[β-D-glucopyranosyl(1→2)-β-D-glucopyranosyl]-dammara-20(22E)-diene-3,12-diol (named as PAN-30).

At page 15, please replace paragraph 43 as follows:

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**[0043]** One or more pharmaceutically acceptable carriers or ~~exipients~~ excipients may be used to formulate pharmaceutical compositions of the invention, including solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic

and absorption delaying agents, and the like that are physiologically compatible. In alternative embodiments, the carrier may be suitable for parenteral, intravenous, intraperitoneal, intramuscular, sublingual or oral administration. Pharmaceutically acceptable carriers may include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the pharmaceutical compositions of the invention is contemplated. Supplementary active compounds can also be incorporated into the pharmaceutical compositions.

At page 17, please replace Example 1 as follows:

**Example 1: Preparation process of producing PAM-120, ~~PBM-100~~ PBM-100, and PAN-20**

- [1] Ginseng crude extract 10 g was dissolved in 40 mL of 95% ethanol
- [2] Add 40 mL of 5 N NaOH
- [3] Pour into the reaction tank, and set temperature to 240°C, and pressure to 3.5 Mpa, for 1.5 hours
- [4] Reduce temperature to room temperature, and take the products out the tank
- [5] Add HCl to neutralize pH to about 7, and expend the volume to 800 mL using water
- [6] Extract 3 times with acetic ester, 100 mL each time
- [7] Combine all the extracts, and reduce the pressure to dry. Thus, obtain 3.8 g of dried extracts
- [8] Grind and dissolved the extract in 20 mL of methanol, and mix the methanol solution with silica gel
- [9] Dry up the mixture, and then grind to fine powder
- [10] Load the Silica gel column
- [11] Wash the column with 60 mL of ether:petroleum benzin (1:3), and thus, 250 mg of PAM-120, and 45 mg of PBM-100 were obtained
- [12] Wash the column with 90 mL of ~~chloroform:methanol~~ chloroform:methanol (95:5), and thus 50 mg of PAN-20 was obtained.

At page 18, please replace paragraph 46 as follows:

**[0046]** Composition: 20(S)-Rh2 was provided by Shenyang Pegasus Pharmaceutical R&D Co., China, with a purity of over 98%. The molecular weight for Rh2 was

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622.3. Sapogenins PAM-120, PBM-100 and PAN-30 were derived from the process stated in Example 1. The molecular weights of PAM-120, PBM-100 and PAN-30 were ~~erspectively~~ respectively 442.7, 474.7 and ~~604.9~~ 766.6, and the purity for each of the three agents was higher than 99%. Rh2, PAM-120, PBM-100 and PAN-30 were dissolved 1 gram each separately in 100 mL absolute ethanol and stored at 4°C. the agents were diluted with RPMI-1640 medium to the desired concentrations as shown in Table 1.

At page 23, please replace paragraph 56 as follows:

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[0056] Figure 2 illustrates a graph of tumor inhibiting effect of various ginsenosides on drug resistant human breast cancer cells MCF7r. Human drug resistant breast cancer cells (MCF7r) were cultured with DMEM and 5% serum supplement in 96-well dishes. Cells were then treated with various concentrations of ~~PAN-20, PAN-10, PAN-12 and Hr2~~ PAN-30, PBM-100, PBM-110, PBM-120, and Rh2, respectively. The number of alive cells were measured using MTT method 24 hours after the treatment and compared with the control samples. All new compounds showed a significantly higher tumor inhibitory effect than Rh2, especially at low concentrations ( $p < 0.01$ , Student t test).